



## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference BCS 03-5005-PCT	<b>FOR FURTHER ACTION</b>		See Form PCT/PEA/416
International application No. PCT/EP2004/010984	International filing date (day/month/year) 29.09.2004	Priority date (day/month/year) 30.09.2003	
International Patent Classification (IPC) or national classification and IPC C12N5/10, A01H5/00, C12N15/82, C12N9/10			
Applicant BAYER CROPSCIENCE GMBH et al.			
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 9 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau) a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>			
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>			
Date of submission of the demand  09.07.2005		Date of completion of this report  21.09.2005	
Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016		Authorized Officer  Holtorf, S  Telephone No. +31 70 340- 	

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International application No.  
PCT/EP2004/010984

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**Box No. I Basis of the report**

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1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
  - ☐ publication of the international application (under Rule 12.4)
  - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements\*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

**Description, Pages**

1-49 as originally filed

**Claims, Numbers**

1-26 as originally filed

**Drawings, Sheets**

1/44-44/44 as originally filed

☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing (*specify*):
  - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing (*specify*):
  - ☐ any table(s) related to sequence listing (*specify*):

\* If item 4 applies, some or all of these sheets may be marked "superseded."

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**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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**1. Statement**

Novelty (N)	Yes: Claims	4,15
	No: Claims	1-3,5-14,16-26
Inventive step (IS)	Yes: Claims	
	No: Claims	1-26
Industrial applicability (IA)	Yes: Claims	1-26
	No: Claims	

**2. Citations and explanations (Rule 70.7):**

**see separate sheet**

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**Supplemental Box relating to Sequence Listing**

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**Continuation of Box I, item 2:**

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:
  - a. type of material:
    - ☒ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☒ in written format
    - ☒ in computer readable form
  - c. time of filing/furnishing:
    - ☒ contained in the international application as filed
    - ☐ filed together with the international application in computer readable form
    - ☐ furnished subsequently to this Authority for the purposes of search and/or examination
    - ☐ received by this Authority as an amendment on
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional observations, if necessary:

1. The following documents are considered relevant for the current application:

D1: EP1103617

D2: Kortstee, A.J., et al., 1998, Carbohydrate Polymers, 37,2,pp. 173-184

D3: WO9634968

D4: EMBL database, Accession No. BG886850

D5: UniProt Database, Acc. No. Q8GWK4 & EMBL database Acc. No. AK118785

D6: Blauth, S.L., et al., 2002, PMB, 48, 3, pp. 287-297

D7: Blauth, S.L., et al., 2001, Plant Phys., 125, 3, pp. 1396-1405

D8: Flipse, E., et al., 1996, 198, pp. 340-347

**Re Item V.**

**2. Novelty and Clarity (Art. 33(2) and Art. 6 PCT)**

2.1 The current application is dealing with the provision of a method for the modification of the amylose/amylopectin ratio in transgenic plants through increasing the activity of a potato "Class 3 branching enzyme".

2.2 As currently drafted, Claim 1 refers to a "genetically modified plant cell" wherein the genetic modification is not further specified and could also be achieved by the use of essentially biological processes like ordinary plant breeding or the selection for mutant plants exhibiting a certain phenotype. Furthermore, said wording does not essentially relate to a plant which has been transformed with a nucleotide sequence encoding a branching enzyme but does indeed refer to any modification leading to an increase in the activity of said branching enzyme. Such modifications of the activity of the branching enzyme can alternatively obtained through the modulation of transcription factors or any other gene/protein interacting in the broadest possible sense with said branching enzyme. Moreover, the term "class 3 branching enzyme" is an internal designation for the identified **putative** potato-specific branching enzyme as characterized by SEQIDs4 and 6. The expression "increased activity" in claim 1 is not further specified and open to any interpretation.

The same objection applies to the dependent claims 5-14,16,17.

2.3 In this respect, any document relating to the sense expression of any branching enzyme in transgenic plants is Novelty destroying for said claims. Document D1 is disclosing the alteration of the amylose/amylopectin ration in plants by expressing a sense construct of a potato branching enzyme. D2 teaches the increasing of the degree of branching in potato plants genetically modified by a sense construct of an E. coli branching enzyme.

Accordingly, the subject matter of claims 1-3,5-14 and 16,17 is not novel over the prior art with respect to Art. 33(2) PCT.

2.4 Kortstee et al. (D2) discloses the analysis of the starch produced in genetically modified potato plants. Due to the lack of any other information characterizing the starch as defined in claims 18-26, said starch as defined in D2 is considered to have the same properties as the starch in claims 18-26.

Consequently, claims 18-26 lack novelty over the prior art with respect to Art. 33(2) PCT.

2.5 When strictly interpreting claims 4g) and 15g), the subject matter of said claims relates to "fragments" and/or "derivatives" of the nucleic acid molecules as defined under a)-e) and f). Such "fragments" are not further defined and could consist of one or two base pairs only.

2.6 Claim 4d) refers to a nucleic acid molecule that has an identity of at least 50% with the nucleic acid sequences as defined under 4a) and 4c). By making reference to 4b) such nucleotide sequence can at least have 50% identity to a nucleotide sequence that encodes a polypeptide exhibiting at the minimum 50% identity to SEQID4. It is doubtful whether such a nucleic acid sequence as defined in 4d) will still have anything in common with a branching enzyme, let alone have the same enzymatic activity.

2.7 The format of the product claims 18,24,25 is unusual. The format is a "product-by-process" format, however, the product steps indicated do not necessarily lead to the product as claimed.

Product claims, as a general rule and if the application allows it, should be defined by the technical features of the product and not by process features.

### **3. Inventive Step (Art.33 (3) PCT)**

3.1 Document D1 is considered to represent the closest prior art and discloses the generation of transgenic potato plants with a modified amylose/amylopectin ratio by utilizing a sense construct harbouring a branching enzyme.

3.2 The difference between D1 and the current application is the use of another potato-specific nucleotide sequence putatively encoding a branching enzyme.

3.3 The problem of the current application is the provision of an alternative branching enzyme for the modulation of the amylose/amylopectin ration in plants.

3.4 The solution is the provision of potato-specific nucleotide sequences encoding a putative branching enzyme as characterized by SEQIDs 3,5 and 4,6, respectively.

3.5 Methods for using potato branching enzymes for the modulation of the amylose/amylopectin ratio in transgenic plants are already known, see D1, D2 and D3. Furthermore, alternative nucleotide sequences encoding alternative branching enzymes are also known, see D4 and D5. Document D4 is disclosing an EST sequence that exhibits 99% identity in 640 Bp to SEQIDs 3 and 5. Faced with the identified problem to provide alternative potato-specific nucleotide sequences encoding branching enzymes, the person skilled in the art would undoubtedly have screened the publicly available sequence databases and come across the EST sequence as defined in D4. Said EST sequence can easily be used as a tool to probe potato cDNA libraries and to finally isolate the respective full-length cDNA. The use of the gene to generate transgenic plants and evaluate the effect of the respective enzyme on the amylose/amylopectin ratio in said plants is obvious in the light of the prior art and not inventive.

Accordingly, the subject matter as defined in claims 1-26 lacks inventive step according to Art.33 (3) PCT.

#### **4. Sufficiency of Disclosure and Support (Art. 5 + 6 PCT)**

4.1 The description does not provide sufficient technical information to enable a skilled person to carry out the invention with respect to the subject-matter of claims 1-26.

4.2 The technical problem stated by the applicant is to provide a method to modify the amylose/amylopectin ratio of plants through the use of a newly identified branching enzyme from potato that appears to belong to a novel class of branching enzymes.

4.3 The description provides experimental evidence for the identification of the nucleotide sequence encoding said branching enzyme and the generation of transgenic rice plants transformed with a sense expression cassette harbouring said gene. However, the description does not provide any experimental evidence providing technical proof that the nucleotide sequence is encoding an active enzyme exhibiting branching enzyme specific activity. Furthermore, the specification is silent about the obtained modifications in starch properties in said transgenic plants.

5.3 In the lack of these technical data and in the light of documents D6-D7 that disclose the generation of transgenic plants wherein the utilized starch branching enzyme has no if any pronounced effect on starch properties and doubts are cast on the role of said enzymes in the biosynthesis of starch, it is not clear whether the branching enzyme as utilized in the current application is representing an active enzyme and the stated problem has been solved. Thus, a person skilled in the art would have to find out if and under which circumstances the method works at all for the identified alternative branching enzyme. Consequently, in the absence of any evidence on the basis of a common general knowledge or on the basis of the application, the subject-matter of all claims referring to the use of said alternative branching enzyme in methods to influence the starch properties in transgenic plants and referring to indirectly influencing the putative activity of said enzyme by the foreign nucleic acids as defined in claim 5 and 16 and to the obtained putatively modified starch and its use is insufficiently disclosed with respect to Art. 5 PCT. For the same reason the said claims lack support (Art. 6 PCT).



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(SEPARATE SHEET)**

International application No.

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